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Review Articles

The relationship between asthma and self-reported anxiety in a predominantly healthy adult population

Elan Gada, MD^{*}; David A. Khan, MD^{*}; Laura F. DeFina, MD[†]; and E. Sherwood Brown, MD, PhD[‡]

^{*} Department of Internal Medicine, The University of Texas Southwestern Medical Center, Dallas, Texas

[†] The Cooper Institute, Dallas, Texas

[‡] Department of Psychiatry, The University of Texas Southwestern Medical Center, Dallas, Texas

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ABSTRACT

Background: Numerous studies involving patients with severe asthma have cited a relation between asthma and anxiety; this relation is responsible for decreased quality of life, increased morbidity, and higher health care usage. However, whether a link between milder asthma and anxiety exists remains unclear.

Objective: To determine whether asthma and anxiety share an association in a group of predominantly healthy adults.

Methods: Adults seen at the Cooper Clinic in Dallas, Texas from March 2000 through January 2013 for preventive medical examinations that included an extensive medical history, including a questionnaire regarding anxiety history, a physician-based physical examination, and laboratory and spirometric testing were used in the analysis. Multiple logistic regressions were used to determine the relation between asthma and anxiety.

Results: The sample consisted of 15,675 patients, of whom 1,403 (9%) had an asthma diagnosis. A sizeable majority of patients with asthma rated their health good or excellent, did not use an inhaler, and had a ratio of forced expiration volume in the first second to forced vital capacity greater than 70%. When controlling for covariates, milder asthma was significantly associated with anxiety (odds ratio 1.435, 95% confidence interval 1.238–1.663, $P < .001$). Smoking, a variable associated with asthma severity, was significantly associated with anxiety (odds ratio 1.432, 95% confidence interval 1.261–1.626, $P < .001$), although other variables, such as the ratio of forced expiration volume in the first second to forced vital capacity or use of an inhaled corticosteroid or combined inhaled corticosteroid and a long-acting β agonist, were not significantly associated with anxiety.

Conclusion: In this cohort of patients with predominantly mild asthma, there was a 43.5% increased risk of anxiety. All patients with asthma should be considered at a higher risk of anxiety and a target population for anxiety screening.

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Introduction

Asthma, a chronic inflammatory lung disease characterized by reversible airflow obstruction and airway hyper-responsiveness, is increasing in prevalence worldwide. Global estimates suggest that there are approximately 300 million people with asthma,¹ with an additional 100 million expected by 2025.² From 2002 through 2007, the cost of asthma was higher than \$3,000 annually per person.³ A significant portion of total expenditures has been attributed to emergency room use, hospitalization, and death.⁴ Appropriate control of asthma remains the highest goal,² because good

management of this disease can result in increased quality of life, decreased morbidity, and lower health care costs.⁵

Anxiety disorders are characterized by feelings of stress or worry about everyday events and activities. Global estimates of the current prevalence of anxiety disorders range from 5.3% to 10.4%.⁶ The total annual cost of anxiety disorders in 2 studies from the late 1990s was estimated to be more than \$40 billion.^{7,8} Anxiety disorders have been associated with several chronic medical conditions, including coronary heart disease,⁹ diabetes,¹⁰ chronic obstructive pulmonary disease,¹¹ and asthma.¹² The role of anxiety disorders in these conditions, particularly asthma, remains to be fully elucidated.

Several studies involving patients with severe asthma have reported a relation between asthma and anxiety.^{12–16} The literature on associations with asthma and anxiety in patients with milder asthma is not as robust. Two smaller studies found no significant differences in the psychological characteristics or prevalence of

Reprints: E. Sherwood Brown, MD, PhD, Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd, MC 8849, Dallas, TX 75390-8849; E-mail: sherwood.brown@utsouthwestern.edu.

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anxiety disorders in patients with mild asthma vs severe asthma.^{17,18} Goodwin et al¹² noted lifetime nonsevere asthma to be associated with an increased odds of any anxiety disorder (odds ratio [OR] 1.51, 95% confidence interval [CI] 1.0–2.32, $P < .05$).¹²

The Cooper Clinic is a preventive medical center in Dallas, Texas, which presents an opportunity to investigate a population of predominantly healthy individuals who extensively report their medical history and undergo screening pulmonary function testing. Using this cohort, the authors sought to evaluate the relation between less severe asthma and anxiety.

Methods

From March 2000 through January 2013, 15,675 generally healthy adult patients were seen at the Cooper Clinic for preventive medical examinations that included an extensive medical history, physician-based physical examination, laboratory testing, and spirometry. Participants gave informed consent for the use of their data in the Cooper Center Longitudinal Study database maintained by the Cooper Institute and approved by the institute's institutional review board.

Assessments

Anxiety screen

Anxiety was assessed based on a yes-or-no questionnaire. The question was “please indicate whether you have ever had a significant problem with anxiety.”

Asthma

Asthma and other common medical conditions were screened for as part of routine clinical assessment at the Cooper Clinic using the statement, “please indicate whether you have ever had a significant problem with any of the symptoms or conditions listed below.” A positive response was confirmed by a physician. Currently prescribed asthma medications were categorized as inhaled corticosteroid (ICS) or combined inhaled corticosteroid and long-acting β agonist (ICS/LABA).

Spirometry

The KoKo PFT System (nSpire Health, Inc, Longmont, Colorado) was used to measure lung function, with the best of 3 trials recorded in the database. Hankinson prediction equations were used to calculate the percentage of predicted forced expiratory volume in the first second (FEV₁) and forced vital capacity (FVC). The FEV₁/FVC ratio was used to determine the presence of obstruction, with scores lower than 70% indicating obstructive physiology.

Health rating

The global health rating of each patient was assessed as part of routine care, using a 4-point (poor, fair, good, or excellent) self-report assessment developed for clinical assessment by the Cooper Clinic.

Statistical analysis

Multiple logistic regression analysis predicted the dependent variable of anxiety (yes, no) based on independent variables of asthma (eg, demographic/health information, pulmonary function values). SPSS 14.0 (SAS Institute, Cary, North Carolina) was used for all analyses, including the summary statistics analyzed using χ^2 tests.

Results

Of 15,675 patients, 1,403 (9%) had an asthma diagnosis. Participant characteristics are listed in Table 1 for those with and without asthma. In general, patients at the Cooper Clinic composed a predominantly male, white, well-educated, nonsmoking patient population. Patients with asthma were slightly younger ($P = .002$), reported lower self-reported health ratings ($P < .001$), and had

Table 1

Demographic information of participants (N = 15,675), Cooper Center

Variable	Asthma group (n = 1,403)	Nonasthma group (n = 14,272)	P value
Men	958 (68.3%)	10,029 (70.3%)	.126
Women	445 (31.7%)	4,243 (29.7%)	
White	1,311 (93.4%)	13,472 (94.4%)	.145
Nonwhite	92 (6.6%)	800 (5.6%)	
Age <50 y	738 (52.6%)	6,898 (48.3%)	.002
Age $\geq$ 50 y	665 (47.4%)	7,374 (51.7%)	
College educated	1,391 (99.1%)	14,183 (99.4%)	.293
No college education	12 (0.9%)	89 (0.6%)	
Nonsmoking	1,248 (89.0%)	12,508 (87.6%)	.160
Smoking	155 (11.0%)	1,764 (12.4%)	
Health rating good, excellent	1,061 (75.6%)	11,788 (82.6%)	<.001
Health rating poor, moderate	342 (24.4%)	2,484 (17.4%)	
BMI $\geq$ 25 kg/m ²	943 (67.2%)	9,191 (64.4%)	.036
BMI <25 kg/m ²	460 (32.8%)	5,081 (35.6%)	
ICS and/or ICS/LABA	215 (15.3%)	43 (0.3%)	<.001
Neither ICS nor ICS/LABA	1,188 (84.7%)	14,229 (99.7%)	
FEV ₁ /FVC <70%	223 (15.9%)	759 (5.3%)	<.001
FEV ₁ /FVC $\geq$ 70%	1,180 (84.1%)	13,513 (94.7%)	

Abbreviations: BMI, body mass index; FEV₁, percentage of predicted forced expiratory volume in the first second; FVC, forced vital capacity; ICS, inhaled corticosteroid; ICS/LABA, combined inhaled corticosteroid and long-acting β agonist.

higher body mass indices ($P = .036$). They more often listed ICS or ICS/LABA use ($P < .001$) and had evidence of obstruction at pulmonary function testing ($P < .001$). Most patients with asthma appeared to have relatively mild asthma. Only 15.3% of patients were on an ICS or ICS/LABA controller. In addition, only 15.9% of patients with asthma had evidence of obstruction on spirometry.

Table 2 presents the association between asthma plus other predictor variables and anxiety. When controlling for the noted covariates, asthma was significantly associated with anxiety (OR 1.435, 95% CI 1.238–1.663, $P < .001$). Smoking, a variable potentially associated with asthma severity, was significantly associated with anxiety (OR 1.432, 95% CI 1.261–1.626, $P < .001$), although other variables, such as the FEV₁/FVC ratio or use of an ICS or ICS/LABA, were not significantly associated with anxiety in this model. There was a significant association between being white and having anxiety (OR 1.429, 95% CI 1.169–1.748, $P < .001$), as has been observed in a previous study.¹⁹ As might be expected, there also was a significant association between health rating and anxiety (OR 0.369, 95% CI 0.334–0.409, $P < .001$). Consistent with another study,²⁰ women had more than twice the risk of anxiety as men.

Discussion

This study shows a significant association between asthma and anxiety in adults, most of whom appeared to have relatively mild

Table 2

Logistic regression model of anxiety from the Cooper Longitudinal Study

Variable	OR	Lower 95% CI	Upper 95% CI	P value
History of asthma	1.435	1.238	1.663	<.001
Women vs men	2.558	2.321	2.82	<.001
White vs nonwhite	1.429	1.169	1.748	.001
Age <50 vs $\geq$ 50 y	0.896	0.541	1.485	.67
College educated vs no college education	0.896	0.541	1.485	.67
Smoking vs nonsmoking	1.432	1.261	1.626	<.001
Health rating good, excellent vs poor, moderate	0.369	0.334	0.409	<.001
BMI $\geq$ 25 vs <25 kg/m ²	0.912	0.825	1.009	.074
ICS and/or ICS/LABA vs neither ICS nor ICS/LABA	1.296	0.947	1.773	.106
FEV ₁ /FVC <70% vs $\geq$ 70%	0.974	0.814	1.165	.773

Abbreviations: BMI, body mass index; CI, confidence interval; FEV₁, percentage of predicted forced expiratory volume in the first second; FVC, forced vital capacity; ICS, inhaled corticosteroid; ICS/LABA, combined inhaled corticosteroid and long-acting β agonist; OR, odds ratio.

asthma. In the present sample, 9% of patients screened had asthma, which approaches the rates of asthma in adults in the United States.¹ However, owing to the preventive nature of the present sample, disease prevalence is likely underestimated. This study had several strengths, including a large sample and use of a control group. It measured a wide range of asthma morbidity variables, including self-reported symptoms, and used a physician-based assessment of asthma and asthma severity. It used objective measurements, such as spirometry, to aid in this calculation. Moreover, because of the range and depth of these assessments, the authors could control for some potential confounders, including asthma severity, smoking status, and major depressive disorder.

To the authors' knowledge, the only other study to objectify the association between less severe asthma and anxiety in an epidemiologic sample was performed by Goodwin et al.¹² Their study was set in Germany and included more than 4,000 adult patients, of whom 236 were given a physician diagnosis of asthma and 143 were classified as having lifetime nonsevere asthma. Overall, their sample included a larger proportion of women than men. Patients were screened for different mental health disorders using a formal interview and examination survey and dichotomized into severe and nonsevere asthma groups based on the interpretation of the study physician. In contrast, the present study included more than 16,000 adult patients, most of whom were men and 1,403 had a physician diagnosis of asthma. Anxiety was screened for using an item on a questionnaire. Patients were thought to have less severe asthma based on a subjective health rating, FEV₁/FVC ratio, and current use of ICS or ICS/LABA. Interestingly, the findings of Goodwin et al are similar to the present findings in that lifetime nonsevere asthma was consistently associated with an increased odds of any anxiety disorder (OR 1.51, 95% CI 1.0–2.32, $P < .05$). The present study showed a similar finding in patients with less severe asthma (OR 1.435, 95% CI 1.238–1.663, $P < .001$).

Asthma is associated with different stress-related disorders, including panic disorder,²¹ generalized anxiety disorder,²² post-traumatic stress disorder,²³ and depression.²⁴ Although the pathophysiology behind the link between asthma and anxiety remains to be fully elucidated, theories involve psychological and biochemical explanations, including the panic fear theory,²⁵ hypothalamic–pituitary–adrenal axis dysregulation leading to altered inflammatory responses in response to asthma triggers,²⁶ and medication effects.²⁷ The link between asthma and anxiety has been associated with increased symptom perception,²⁸ decreased quality of life,^{29,30} increased emergency room visits,³⁰ increased primary care visits,^{29,30} increased medication requests,³¹ increased β -agonist use,²⁹ and higher health care usage.^{29,32,33} Many of these findings have been based on studies including patients with severe asthma. However, no studies to the authors' knowledge have exclusively investigated the behavioral and medical consequences of less severe asthma and anxiety; this remains an important area of investigation. Significant correlations might suggest that screening and treatment for anxiety in mild asthma may need to be used at an earlier stage of disease. There are no current guidelines to suggest when to screen for or treat anxiety in patients with asthma, although cognitive behavioral therapy,³⁴ physiotherapy involving breathing exercises,³⁵ and serotonergic medications³⁶ have been used with some treatment benefit. Lifestyle modification will continue to be an important area of management; for example, in the present study, smoking, which has been associated with worse asthma control,³⁷ was associated with anxiety in patients with mild asthma.

This study has some limitations. First, the study design was cross-sectional. Longitudinal studies may be helpful in determining when patients with less severe asthma develop anxiety, thereby indicating an appropriate time to screen for and treat anxiety in these patients. Second, patients were recruited from a single center and this study population was predominantly white. Although the

limited sample heterogeneity may increase the internal validity of the study, it also may decrease the generalizability of the findings. Third, anxiety is more common in women, although this sample consisted largely of men. Although this may have been a potential bias, 4,688 women were included in this study and sex was controlled for in the analysis. Fourth, anxiety was not assessed using a validated questionnaire, but rather based on a single response as part of a screening questionnaire designed for clinical use. It is important to note that the diagnosis of anxiety requires a more comprehensive assessment than could be performed in this study. However, the perception of anxiety in patients with asthma remains a significant aspect of their disease.³⁸ Fifth, although an asthma diagnosis was confirmed by a clinic physician, the patients were not assessed by an allergist or pulmonologist. Sixth, although a physician assessment was part of the assessment process, disorders such as hyperventilation and psychogenic dyspnea can mimic asthma and could not definitively be ruled out, although the overall prevalence of asthma was comparable to that reported in the United States.¹ Seventh, there was a low prevalence of patients with obstructive lung defects and patients using controller medications in this generally healthy population. Thus, this study may have been underpowered to detect an association between FEV₁ and FEV₁/FVC and controller medication use in patients with relatively mild asthma and anxiety. Alternatively, an association between asthma severity and anxiety may not be present, because 2 previous studies have not identified such an association.^{38,39} Eighth, an obstructive defect was defined based on a FEV₁/FVC ratio lower than 70%, which may have led to a falsely larger number of patients among elderly patients or a falsely smaller number of patients among younger adult patients classified as having obstruction. Despite these limitations, in this large population, a significant relation between milder asthma and anxiety was identified.

In summary, an increased risk of anxiety was observed in a relatively healthy group of patients with asthma. The findings are strikingly similar to those of a study by Goodwin et al.¹² Longitudinal studies are needed to determine the duration and course of anxiety symptoms in patients with asthma and to elucidate the clinical correlates and possible mechanisms.

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